REMARKS

Claims 1-29 and 32-65 are pending, claims 58-65 having been added and claims 30 and 31 having been canceled by the present amendment. Claims 1 and 2 have been amended. The amended and new claims are supported throughout the application as filed, e.g., at page 25, lines 2-5; page 27, lines 17-27; and by original claim 30 (now canceled). No new matter has been added. Claims 12-25 and 34-57 are withdrawn from consideration as drawn to non elected claims or species. Claims 1-11, 26-29, 32, 33 and 58-65 are currently under examination.

As presently amended, claims 1-11, 26-29, 32 and 33 are directed to a method for identifying a subunit specific modulator of the N-methyl-D-aspartate (NMDA) receptor. The method includes (a) providing a plurality of recombinant NMDA receptors which differ in their subunit identity; (b) contacting the NMDA receptors with a neurotransmitter recognition site ligand in the presence and absence of a steroid-based candidate modulator; and (c) assaying for receptor activity. An increase or decrease in a subset of the NMDA receptors in the presence of a candidate modulator is an indication that the candidate modulator is subunit specific. New claims 58-65 are directed to a method for identifying a subunit specific modulator of the NMDA receptor, which method includes (a) providing a plurality of NMDA receptors which differ in their subunit identity; (b) contacting the NMDA receptors with a neurotransmitter recognition site ligand in the presence and absence of a candidate modulator obtained from a library of small molecules; and (c) assaying for receptor activity. An increase or decrease in a subset of the NMDA receptors in the presence of a candidate modulator is an indication that the candidate modulator is subunit specific.

Election/Restriction

Applicants affirm the election of species A (NMDA receptors with identical NR2 subunits and different NR1 subunits) within Group I.

Objections to the Specification and Drawings

The disclosure is objected to because of various informalities. The specification has been amended merely to spell out certain art-recognized abbreviations, as noted by the Examiner, and to correct the numbering of the Figures in the Description of the Drawings, as required by the Examiner. No new matter has been added.

The drawings are objected to for various informalities. A proposed drawing correction of Figure 1 is being submitted herewith, as required by the Examiner. Items 6, 10 and 12 in the Notice of Draftperson's Patent Drawing Review will be addressed upon submission of formal drawings under separate cover.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 2 is rejected as being indefinite for having insufficient antecedent basis for the phrase "the subset of the NMDA receptors." Claim 2 has been amended to recite elements having proper antecedent basis in claim 1. Therefore, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

Park-Chung et al., Mol. Pharmacol. 52:1113-1123, 1997 (Park-Chung).

Claims 1, 2 and 26-33 are rejected as allegedly anticipated by Park-Chung. Claims 30 and 31 have been canceled. This rejection is respectfully traversed insofar as it may be applied to the presently amended claims. As amended, claim 1 recites "providing a plurality of recombinant NMDA receptors which differ in their subunit identity." Claims 2, 26-29 and 32-33 depend directly or indirectly on claim 1, and thus contain the same limitation. Park-Chung discloses experiments in which the effect of neurosteroids is evaluated on native NMDA receptor (from chick spinal cord and rat hippocampus) and on a single recombinant NMDA receptor having $NR1_{100}$/NR2A subunit composition (see, e.g., Park-Chung, summary, first full paragraph of page 1114, and first full paragraph of page 1119). Park-Chung does not disclose or suggest a plurality of recombinant NMDA receptors that differ in subunit identity. Accordingly, Park-Chung does not anticipate the present claims.

With regard to the new claims, claim 58 is based on original claim 32, written as an independent claim. Park-Chung clearly does not disclose obtaining a candidate modulator from a library of small molecules, as recited in claim 32. Therefore, Park-Chung cannot be said to anticipate either claim 32 or new claim 58 and its dependencies.

Durand et al., PNAS USA 89:9359-9363, 1992 (Durand)

Claims 1, 2, 26-29 and 31-33 are rejected as allegedly anticipated by Durand. This rejection is respectfully traversed insofar as it may be applied to the presently amended claims. As amended, claim 1 requires that the candidate modulator be a steroid-based molecule. Durand discloses experiments in which the potentiating effect of polyamine, spermine and PKC activators is evaluated on two types of homomeric NMDA receptors in oocytes. Nowhere does Durand disclose or suggest evaluating the effect of steroid-based molecules. Therefore, Durand does not anticipate the current claims.

Neither does Durand disclose obtaining a candidate modulator of NMDA receptors from a library of small molecules, as recited in claim 32. Therefore, Durand does not anticipate new claims 58-65.

Williams et al., Mol. Pharmacol. 45:803-809, 1994 (Williams); Daggett, U.S. Patent No. 5,849,895 (Daggett); Masuko et al., Mol. Pharmacol. 55:957-969, 1999 (Masuko); Traynelis, J. Neurosci. 18:6163-6175, 1998 (Traynelis)

Claims 1-6, 26-28, 31 and 33 are rejected as allegedly anticipated by Williams. Claims 1-5, 7, 26-29 and 31 are rejected as allegedly anticipated by Daggett. Claims 1-5, 8, 26-29, 31 and 33 are rejected as allegedly anticipated by Masuko et al. Claims 1-6, 8, 11, 26-28, 31 and 33 are rejected as allegedly anticipated by Traynelis. As discussed above, the present claims are directed to testing the subunit specificity of a steroid-based molecule on NMDA receptor activity. Neither Williams, Daggett, Masuko nor Traynelis disclose testing the effect of a steroid-based molecule on a plurality of recombinant NMDA receptors which differ in their subunit identity, as required by the claims. Therefore, the present claims are not anticipated by these references.

In light of the present amendments to the claims and the foregoing remarks, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

Claim 9 is rejected as being unpatentable over Daggett in view of Masuko. This rejection is respectfully traversed insofar as it may be applied to the present claims. As a first step to establish prima facie obviousness of a claimed invention, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." (See MPEP § 706.02(j), emphasis added). As discussed above, neither Daggett nor Masuko, alone or in combination, disclose or suggest all the limitations of claim 1 (upon which claim 9 depends). Specifically, neither Daggett nor Masuko, alone or in combination, disclose or suggest testing the subunit specificity of a steroid-based molecule on NMDA receptor activity. Accordingly, the present claims are not obvious over the cited references. Therefore, Applicants respectfully request that this rejection be withdrawn.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a Petition for Extension of Time with a check for the required fee. Please apply the fee for excess claims and any other charges or credits to Deposit Account No. 06-1050, referencing the attorney docket number 13594-010002.

Respectfully submitted,

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